Technology Sciences Group Inc.
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Gary J. Burin, Ph.D., DABT
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GRN 000552

November 6, 2014

Leah Rosenfeld, Ph.D.
US FDA
CFSAN
5100 Paint Branch Parkway, HFS-255
College Park MD
20740

Dear Dr. Rosenfeld,

On behalf of BioAmber Inc., I hereby notify the Agency of our determination on the basis of scientific procedures that BioAmber's succinic acid manufactured from fermentation is generally recognized as safe (GRAS) for the uses and use levels identified in 21 CFR 184.1091, the GRAS affirmation regulation for succinic acid. Three copies of BioAmber's GRAS notification for succinic acid are enclosed.

Please don't hesitate to contact me if you have any questions.

Sincerely,

(b) (6)

Gary J. Burin, Ph.D., DABT

Enclosures

Cc: Laurent Bernier, BioAmber Inc.

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Before the

FOOD AND DRUG ADMINISTRATION

Department of Health and Human Services

Washington DC

GRAS NOTIFCATION

Name of Notifier:	BioAmber Inc.
Post Office Address:	All communications for this matter are to be sent to Gary Burin, Technology Sciences Group Inc., 1150 18th Street NW, Suite 1000, Washington DC 20036
Name of Substance and Intended Use:	Bio-based succinic acid for use as a flavor enhancer and pH control agent
Dated:	November 6, 2014

1. Claim of GRAS Exemption

i. Name and Address of Notifier

BioAmber, Inc.
1250 René Levesque Boulevard West
Montréal, Québec
Canada H3B 4W8

ii. Common or Usual name of notified substance

The common or usual name for the substance is succinic acid. The substance is produced using bio-based technology but is virtually identical to succinic acid currently regulated as generally recognized as safe in 21 CFR 184.1091

iii. Applicable conditions of use

Flavor enhancer or pH control agent

iv. Basis for GRAS determination

The use of bio-based succinic acid is GRAS on the basis of scientific procedures in accordance with 21 CFR 170.30

v. Statement of availability of data

The data and information that are the basis for the GRAS determination are available for the Food and Drug Administration's review and copying and can be sent to FDA upon request.

The foregoing and attached information considered, it is respectively submitted that the use of bio-based succinic acid prepared as described is generally recognized as safe for use in foods as flavoring agent and is therefore exempt from the pre-market approval requirements of the Federal Food, Drug and Cosmetic Act.

Respectfully submitted,

Bio-amber

By (b) (6)

Gary J. Burin, Ph.D., DABT
Technology Sciences Group Inc.
Agent for the Notifier

REQUEST FOR EXTENSION OF GRAS STATUS TO SUCCINIC ACID PRODUCED BY FERMENTATION

SUBMITTED TO: **Division of Biotechnology and GRAS Notice Review**
Office of Food Additive Safety, US FDA

BY: **BIOAMBER INC.**

DATE: **November 6, 2014**

1. INTRODUCTION

Succinic acid is regulated as a food additive in 21 CFR 184.1091. The regulation states that succinic acid is commercially prepared by hydrogenation of maleic or fumaric acid or by the aqueous alkali or acid hydrolysis of succinonitrile. BioAmber's fermentation technology provides several advantages over derivation from petrochemical sources, including increased efficiency and cost effectiveness and decreased environmental impact.

BioAmber's bio-based succinic acid (Bio-SA®) can be used as a monomer in the production of bioplastics and plasticizers in replacement of petroleum constituents. Succinic acid is a precursor for a number of compounds, including tetrahydrofuran, 1,4-butanediol and γ-butyrolactone. Succinate has a wide variety of potential applications including use in liquid antifreeze, heat transfer fluids, pigments, the polyesters poly-butylene succinate (PBS) and PEIT, synthesis intermediates and plasticizers.

BioAmber's fermentation process and integrated downstream process consume greenhouse gases (CO_2). Its core technology has been proven at a large scale in France (350,000 litres (L)) (www.bio-amber.com).

BioAmber's succinic acid is produced by a proprietary strain of *E. Coli* K12 in their toll manufacturing facility in Bazancourt, France. However, the company will have a fully operational succinic acid plant in Sarnia, Ontario, Canada in the first quarter of 2015 when production will be assured by a recombinant Saccharomycetaceae strain of yeast. The Sarnia manufacturing process is described because production will soon be transferred to that plant. The characterization of succinic acid in the following section was generated using the succinic acid produced in France. The microorganism used, the process and the ensuing product are very similar and the bio-based succinic acid should be considered the same product.

2. CHEMICAL IDENTITY

Product Name	Bio-based succinic acid
Chemical name	succinic acid butanedioic acid
CAS number	110-15-6
EC number	203-740-4

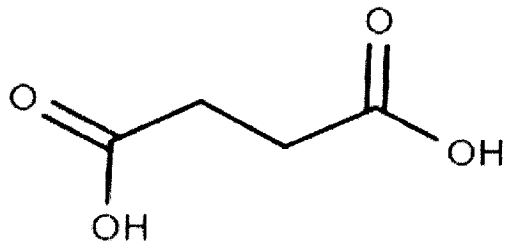

Figure 1. Chemical Structure of Succinic Acid

Succinic acid ($C_4H_6O_4$, CAS Reg. No. 110-15-6), is also known as butanedioic acid. It is a solid at room temperature, has negligible vapor pressure, high water solubility and minimal volatility. It is stable to hydrolysis and photolysis but is expected to degrade at rapid rates by biodegradation.

The succinic acid produced from BioAmber's fermentation process described in this notification is highly purified succinic acid and meets the Food Chemical Codex standards (FCC 9th edition 2014). The major characteristics and components of BioAmber's succinic acid are reported in the table below (Table 1) and the standards cited in the FCC monograph are given in the following table for comparison (Table 2). The product SDS is presented in Appendix 2 for a complete description of its physical/chemical properties.

Table 1. Major characteristics/components of BioAmber's succinic acid

Test	Method	Units	Results
Absorbance at 270 nm	SUC-108-01	Abs	0.013
Acetic acid	SUC-123-02	µg/g	57
Appearance	Visual	--	Colorless or white crystals
Fumaric Acid	SUC-118-01	µg/g	61
Lactic Acid	SUC-122-01	µg/g	16
Melting Point	SUC-104-01	°C	187
Moisture, Karl Fischer	SUC-115-01	µg/g	0.2
pH	SUC-105-01	pH	2.6
Purity	USP Succinic Acid Monograph Assay	%	99.5
Residue on ignition	USP method 281	%	<0.0005

It is important to note that the characteristics of BioAmber's succinic acid do not change significantly from lot to lot that are released to the customer in order to deliver a consistent product.

Table 2. Analysis of Bioamber's Succinic Acid as per US Food Chemicals Codex

Test	Method	Units	Results
Appearance	Visual	--	Colorless or white crystals
Assay	USP Succinic Acid Monograph Assay	%	99.0 – 100.5
Identification	Spectrophotometric identification test, Appendix IIIC	--	Pass
Lead	Lead limit test, Appendix IIIB	mg/kg	≤ 2
Melting Point	Appendix IIB	°C	185.0 – 190.0
Residue on ignition	Appendix IIC	%	≤ 0.025

Given that the succinic acid produced by BioAmber is close to being pure, i.e. ≥99.0%, there are relatively low levels of specific impurities in the product (Tables 1 and 3).

Fumaric, acetic and lactic acids (Table 1) and to a lesser extent, malic and pyruvic acids (Table 3) are produced by fermentation by the microorganism during normal metabolism and may be found at low levels in biobased succinic acid. These molecules have similar structure and are carboxylic (lactic, acetic) or dicarboxylic (succinic, fumaric, malic) acids. Pyruvic acid is a carboxylic acid with an attached ketone.

Each of these acids was given GRAS status by the FDA because of their long history of use and presence in food. Other trace impurities listed below are present under levels of detection by modern

analytical methods. Most are metals that are normally found in water and have been introduced with the water used in the fermentation process. A full analysis was undertaken by Silliker Labs in Markham, Ontario, to determine average levels of heavy metals, pesticides and toxicants in three succinic acid samples. Two hundred and thirty pesticide compounds were tested and all were reported below the detection limit of the test.

Table 3. Trace impurities that can be found in BioAmber's succinic acid (<10 µg/g)

Test	Method	Units	Results
Arsenic	EPA method 6010B	µg/g	<0.49
Cadmium	EPA method 6010B	µg/g	<0.05
Glucose	SUC-127-01	µg/g	<2.8
Iron	EPA method 6010B	µg/g	<2.40
Lead	EPA method 6010B	µg/g	<1.5
Malic Acid	SUC-122-01	µg/g	<10
Mercury	EPA method 7471A	µg/g	<0.05
Pyruvic Acid	SUC-118-01	µg/g	<7
Total Nitrogen	SUC-117-01	µg/g	8
Total Phosphate	SUC-114-01	µg/g	1

BioAmber's succinic acid is virtually identical to the conventional succinic acid and that no difference in functional effectiveness is expected.

3. HISTORY OF USE AND REGULATORY STATUS

Succinic acid is widely used as a flavor enhancer and pH control agent for food. Maximum recommended concentrations for succinic acid added to meat and condiments and relish s are 0.0061 and 0.084 %, respectively. The addition of succinic acid to food is limited to the amount consistent with Good Manufacturing Processes.

Regulatory status – United States

Succinic acid is on the TSCA list of registered substances with number 2517. Succinic acid is Generally Recognized as Safe for use in food as a flavor enhancer and pH control agent (21 CFR 184.1091).

Regulatory status - Canada

Of succinic acid. It is on the Domestic Substances List.

Of the microorganism. The period of assessment by Environment Canada of the New Substance Notification dossier No. 17329 for the BioAmber yeast strain with the additional review of the biosafety level of the strain by the Centre for Biosecurity of the Public Health Agency of Canada (PHAC), is now complete. In summary, PHAC confirms that the strain is a Biosafety level 1 organism and neither PHAC nor Environment Canada found any risk associated with the activities proposed in our notification. This means that BioAmber can import and use the SBA strain in Sarnia for the manufacturing of bio-based succinic acid under the operational and safety procedures mentioned in the notification.

Regulatory status - Europe

Of succinic acid. Submission report UD309022-56 was filed on April 17th 2012 to comply with the European REACH regulation. For this submission, BioAmber was under the obligation to demonstrate that their bio-based succinic acid molecule was the same as the one obtained from a petro chemical

source. A Proton Nuclear Magnetic Resonance (*1H-NMR*) Spectroscopy assay was therefore conducted to demonstrate the equivalency between the two molecules[1].

Note on the microorganism used by ARD, Bazancourt, France, BioAmber's toll manufacturer. At present, the microorganism used for the production of succinic acid is a strain of E. Coli K12. The specifications and characteristics of the finished ingredient presented above are those determined with the succinic acid produced in France. The fermentation process is very similar to the one that will be used with the SBA strain of yeast in BioAmber's plant in Sarnia, therefore the characteristics of the succinic acid produced by the SBA yeast are expected to be similar.

Self-limiting levels of use

Succinic acid is affirmed as GRAS for use as a flavor enhancer under 21 CFR 184.1091 as defined in 170.3(o)(11) and a pH control agent as defined in 170.3(o)(23). The ingredient is used in food at levels not to exceed good manufacturing practice in accordance with 184.1(b)(1). Current good manufacturing practice results in a maximum level, as served, of 0.084 percent in condiments and relishes as defined in 170.3(n)(8) of this chapter and 0.0061 percent in meat products as defined in 170.3(n)(29) of this chapter. Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

4. COSMETICS

Succinic acid is on the International Nomenclature of Cosmetic Ingredients with the following description:

Chem/IUPAC Name / Description:	1,4 Butanediol/Succinic Acid/Adipic Acid/HDI Copolymer is a copolymer of Hexanedioic acid, polymer with butanedioic acid, 1,4-butanediol, and 1,6-diisocyanatohexane
Restriction (applies to EU only):	Last update on 2009 Jul 14 - no restriction
Functions:	1,4 Butanediol/Succinic Acid/Adipic Acid/HDI Copolymer is classified as: ABRASIVE, BINDING, FILM FORMING

5. FOOD

Succinic acid is one of the natural acids found in broccoli, rhubarb, beets, asparagus, fresh meat extracts, sauerkraut and cheese (Furia, 1972). Succinic acid is used in the food and beverage industry, primarily as an acidity regulator.

[1] A sample of bio-based succinic acid was characterized by Nucleic Magnetic Resonance (NMR) 1H and 13C{1H} by FILAB Industrial Analyses Laboratories, Dijon, France, to confirm the identity of the molecule therefore establishing equivalency with the petrol based molecule. The analyses were done with a Bruker NMR 300 MHz spectrometer equipped with a BBOF sensor at ambient temperature (300K). Obtained spectra are representative of the structure of succinic acid samples used as references (SDBS ref 3001). The full report can be found in Appendix 3.

5.1. REGULATORY STATUS

Table 1. Regulatory status of succinic acid in the food industry

COUNTRY	GOVERNING BODY/ LEGISLATION	Status of Succinic Acid	
		As food additive	As a Food Flavor
UNITED STATES	United States Food and Drug Administration	is considered a Food Additive and can be marketed and sold in the US because: Is considered GRAS therefore no further authorization is required for use as a food additive	Since succinic acid is considered a food additive and food flavors are a subset of the food additive group, succinic acid can be marketed and sold as a food flavor in the US.
EUROPE	European Food Safety Authority	Succinic acid is on the list of food additives: E number: E 363 with restrictions. It is authorized in the following categories: a) flavored fermented milk products including hear treated products: ML[2]=6000 mg/L; b) soups and broths : ML=5000 mg/kg; c) flavored drinks, only powders for home preparation of : ML=3000 mg/L; d) Desserts excluding certain category of products : ML=6000 mg/kg	Succinic acid is on the list of food flavorings: FL No. 08.024, for all categories of flavored foods under Legislation: (EU) No. 872/2012. Furthermore, the product can be labeled as 'Natural' according to articles 3(2) (c) and (k) of Regulation (EC) No. 1334/2008 regarding natural flavoring substances.
INTERNATIONAL	Food and Agricultural Organization and World Health Organization	Succinic acid was evaluated at the 29th meeting of the Joint FAO/WHO Committee on Food Additives and Contaminants.	An ADI "not specified" was established for the succinate moiety.

5.2 DIETARY INTAKES

Because the intended uses are identical and bio-based succinic acid meets Food Chemicals Codex specifications no increased expsoures are anticipated from dietary exposure to bio-based succinic acid. The European Food Safety Agency estimated that dietary exposure to succinic acid in Europe in 1,500 micrograms per person per day (EFSA, 2011).

5.3 INTENDED CONDITIONS OF USE

The intended use of the bio-based succinic acid will be as a flavor enhancer and a pH control agent as defined in 21 CFR 170.3(o) (11) and as determined by 21 CFR 184.1091. The intended use of bio-based succinic acid is identical to succinic acid as described in 21 CFR 184.1091.

[2] Maximum Limit

6. MANUFACTURING BIO-BASED SUCCINIC ACID

Yeasts are used as biocatalysts in a number of industrial fermentations (pharmaceuticals, amino acids, vitamins, alcohol, wine, beer, etc.) and have been extensively used throughout history. They present several advantages over bacteria, including resistance to bacteriophage infection, which can lead to loss of productivity or of whole fermentation runs as with bacteria. Until recently, yeast strains that have been developed for succinate production have not exhibited high enough yields, titers and volumetric productivity for economic production at an industrial scale. An improved yeast strain that cost-effectively generates succinate on a large scale is now used for the commercial production of succinic acid.

6.1 BIOAMBER'S PROPRIETARY STRAIN OF MICROORGANISM

Source of the strain

The present strain of yeast used by BioAmber for succinic acid production is called the SBA strain. The SBA strain was developed from a wild-type of *Saccharomycetaceae* strain of yeast isolated from high moisture corn in the US. No sexual reproduction is expected because the strain is an anamorph of the genus. An anamorph is an asexual version of a yeast species while the telomorph is the sexual (perfect state) version.

6.2. DESCRIPTION OF THE BIOLOGICAL AND ECOLOGICAL CHARACTERISTICS OF THE WILD HOST AND SBA STRAIN

Biology, habitat, geographical distribution of the host microorganism

The host strain is widely distributed in nature and has been isolated from various natural habitats including soil, air, sewage, silage and foods. The latter include dairy and meat products, sugar and syrup-based products, wines and beers, cocoa fermentations, rotten fruit, table olives, silage/feeds, wines, beers and various cereal fermentations. It is also found in chickens and seagulls. It is considered a transient commensal in man and has been isolated from the skin and the mucosal surfaces of healthy individuals.

The use of similar yeasts in the food industry

Yeasts extracts such as brewer's yeast have a long history of use in the food industry and more uses are being developed for these microorganisms. The increasing interest in healthy diets stimulated the innovative development of novel products with antioxidant ability in the food industry. These yeasts extracted from dairy products were shown to have excellent antioxidant activity and are recommended for the production of functional foods or natural antioxidant supplements in the food industry. They are present at a low level in spontaneous fermentation of grapes.

6.3 RISKS INVOLVING THE USE OF THE SBA STRAIN

The SBA strain has been altered considerably to produce succinic acid therefore reducing its capacity to perform other metabolic pathways. It has demonstrated a two-fold lower growth rate than the wild host strain (see below). **The conditions required for, and conditions that limit survival, growth and replication of the SBA strain:**

- Upper limit for growth = 45°C, no lower limit known survives at -80C for weeks without cyroprotectant (these data exceptionally pertains to the wild strain);
- Organism can be killed by temperatures >60C for times >1.5 hrs;
- Chemical kill – bleach kill validated at 2% household bleach volume/volume for 60 min.
- Genetically modified strain will not grow in the absence of oxygen.
- Lower growth rate than wild type
- Organism has limited substrate range.

Sensitivity to known antimicrobials

Studies with the SBA strain using several different classes of antifungal agents, (i.e. Polyene: Amphotericin B ; Imidazole: Ketoconazole ; Triazole: Fluconazole ; Echonicandin: Caspofungin ; Nucleic acid analogue: Flucytosine) demonstrated that the SBA strain is susceptible to fluconazole as well as to amphotericin B, flucytosine and ketoconazole and resistant to capsofungin (Dubois and Bernier 2013).

Risk that the SBA strain will have adverse human health effects

There are no documented reports of adverse human health effects of the SBA strain.

SBA strain is not likely to pose a risk to human health, to plants, or to other microorganisms because the host strain has been shown to survive poorly in the environment, has a history of safe commercial use, and is not known to have adverse effects on humans, plants or microorganisms. In general, large scale industrial manufacture of the host strain preparations have a history of safe use in many industries including ethanol production. Based on the criteria outline in the OECD guidelines entitled Recombinant DNA Safety Considerations (OECD 1986) and the European Communities Council Directive 90/219/EEC an following amendment (ECC 1998) on the contained use of genetically modified microorganisms (ECC 1990*), the host strain* can be regarded as a safe host organism.

In summary, the wild host strain is considered a BSL1 microorganism and the BioAmber's SBA strain was given the same status by Health Canada and Environment Canada. The genetic modifications performed to develop SBA strain do not give rise to concerns of altered virulence or pathogenicity to humans, animals, plants or altered hazards to the environment. The phenotype resulting from the modifications is well characterized and is not likely to influence the normal behaviour of the SBA strain.

The system monitoring approach at BioAmber will also be in compliance with regulatory requirements on containment of the microorganism of the BioSafety Level 1 Containment as described in the previous section.

7. EXPOSURE TO SUCCINIC ACID FROM ITS INTENDED USES

Intended use

The intended uses of the bio-based succinic acid will be as a flavor enhancer and a pH control agent. These uses are identical to those described for succinic acid in 21 CFR 184.1091.

Risks related to the substance

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Succinic acid is an organic diacid with 4 C ($C_4H_6O_4$) which is present in numerous metabolic pathways of life forms. Because the intended uses are identical and bio-based succinic acid meets Food Chemicals Codex specifications no increased risk is anticipated from dietary exposure to bio-based succinic acid.

8. SAFETY ASSESSMENT OF SUCCINIC ACID

BioAmber's succinic acid is substantially equivalent to the product made by hydrogenation of maleic or fumaric acid or by aqueous alkali or acid hydrolysis of succinonitrile, which is affirmed as GRAS in 21 CFR 184.1091.

The following is a presentation of studies done with succinic acid since the assessment for GRAS status in 1973 (Informatics inc. 1973) and corresponding work done for FDA and published in 1975 (Litton Bionetics Inc. 1975; Federation of American Societies for Experimental Biology 1975).

United States Environmental Protection Agency High Production Volume Challenge Program. The US EPA reviewed data on succinic acid in 2008 in the context of its High Production Volume (HPV) Challenge Program which entails the identification and initial assessment of the adequacy of existing toxicity data/information in order to provide to the public, information on health and environmental effects of chemicals manufactured in or imported into the US in quantities greater than one million pounds per year (EPA OPPT 2008). Because succinic acid was produced in volumes in the range of 10 to 50 million pounds per year, the product was included in the HPV evaluation.

The information reviewed confirmed that the acute oral toxicity of succinic acid is low. Repeated exposures via oral route affected body weight gains at higher doses. In repeated-dose toxicity studies, no effects on reproductive organs were seen. In developmental toxicity studies, the category members did not show any effects on fetal survival, fetal weight, litter size or implantations, or any skeletal or visceral abnormalities. Succinic acid was not mutagenic in tested strains of *Salmonella typhimurium* as well as in mammalian cells and did not induce statistically significant increase in the mean number of micronucleated polychromatic erythrocytes in the bone marrow of CD-1 mice. In a 2 –year carcinogenicity study of monosodium succinate, tumors were found in many organs or tissues in all groups including the controls. None of the treated groups showed a significant increase in the incidence of any tumors over that in the corresponding controls. Monosodium succinate did not increase the incidence of any tumors over that in the corresponding controls in a 2-year drinking water study. The potential health hazard of the dicarboxylic acid is low based on the available animal data reviewed (EPA OPPT 2008).

The following sections give details on the studies done for the HPV Challenge Program as well as results taken from the literature on the toxicology of succinic acid.

8.1 ABSORPTION, DISTRIBUTION, METABOLISM AND EXCRETION

Succininc acid is formed endogenously as a component of the tricarboxylic acid cycle (Krebs, 1938). High concentrations of succinate promote the activity of succinate dehydrogenation in the cycle

(Leninger, 1975). Succinate is metabolized to fumerate. This reaction is inhibited by oxaloacetate and other intermediates. A complex network controls the rate of carboxylic acid cycle.

8.2 ACUTE TOXICITY

Table 2. Results of acute toxicity studies using succinic acid or similar chemistries

Reference	Short description /Results
Maekawa et al. 1990.	Monosodium succinate was dissolved in distilled water. Groups of 4 male and 4 female rats were given, by stomach tube, a single dose of 0.5, 1, 2, 4, or 8 g monosodium succinate/kg body weight. Oral LD50> 8 g/kg
Lewis, 1996	LD50 Rat oral 2260 mg/kg

8.3 SUBCHRONIC (REPEATED DOSE) TOXICITY

Table 3. Results from subchronic or repeated dose studies using succinic acid or similar chemistries

Reference	Short description /Results
Thind et al. 1980	Administration of 500 mg/100g/day of succinic acid for 20 days to rats 60 days post-operative after induction of bladder stone formation. Stone formation was seen in 36% of animals treated with succinic acid and, 60% of control animals.
Maekawa et al. 1990.	In a 13-week study, groups of male and female F344 rats were administered monosodium succinate at 0, 0.3, 0.6, 1.25, 2.5, 5 and 10% (approximately 0, 300, 600, 1250, 2500 and 10,000 mg/kg-bw/day) in their drinking water. All animals in the 10% group showed severely decreased body weight gain (severely emaciated) and died within the first 4 weeks of the study. The decreased body weight gain was also seen at and above 2.5%. No effects were seen on hematological or biochemical parameters. No treatment-related histological lesions were seen in any organ, although atrophy of organs was noted. LOAEL = 2.5% (~2500 mg/kg-bw/day; based on severely decreased body weight gain). NOAEL = 1.25% (~1250 mg/kg-bw/day)

8.4 DEVELOPMENTAL AND REPRODUCTIVE TOXICITY

Table 4. Results from developmental studies using succinic acid

Reference	Short description /Results
Verrett et al. 1980.	Fresh fertile eggs were used. The test material was administered by a single injection in a volume of 100 µL or less, and solvent controls were treated with the same volume of the solvent (water) only. For each injection route, eggs were treated at 2 stages of incubation: preincubation (0 hour) and at the 4th day (96 hours). Hence there were 4 test conditions for the test substance. Groups of 20 or more eggs were treated under these 4 conditions at a minimum of 5 dose levels until a total of approximately 100 eggs per level was reached for all levels that allowed some chicks to hatch. Groups of comparable size were treated with the vehicle at corresponding volumes, and untreated controls were also included in each experiment. Succinic acid had an LD50 of 0.32 mg/egg in the air cell at 96 hours. The highest level tested was 2.5 mg/egg. No teratogenic effects were observed in the developing chicken embryo.
Ain and Seshagiri 1997.	The influence of succinate on the development of hamster 8-cell embryos to blastocysts was examined using a chemically defined protein-free modified hamster embryo culture medium-2 (HECM-2m). There was a dose-dependent influence of succinate on blastocyst development; 0.5 mM was optimal. The data showed that supplementation of succinate to HECM-2m supports 100% development of hamster 8-cell embryos to high quality viable blastocysts, and that non-glucose oxidizable energy substrates are the most preferred components in hamster embryo culture

	medium.

8.5 CARCINOGENICITY

Table 5. Results from carcinogenicity studies using succinic acid or similar chemistries

Reference	Short description /Results
Maekawa et al. 1990.	In a 2-year carcinogenicity study, male and female F344 rats were administered monosodium succinate in drinking water at 0, 1 and 2% (~1000 or 2000 mg/kg-bw/day). After 104 weeks of treatment, the rats were given distilled water for additional 9 weeks and then sacrificed at week 113. The test substance intake was 196 and 437 mg/rat/day for males and 146, and 309 mg/rat/day for females, at 1 and 2%, respectively. Treatment- and dose-dependent decreases in growth rate were seen. In both sexes, there were no statistically significant differences between the control and treated groups in overall tumor incidences and mean survival times. Tumors were found in many organs or tissues in all groups including the controls. None of the treated groups showed a significant increase in the incidence of any tumors over that in the corresponding controls. Monosodium succinate did not increase the incidence of any tumors over that in the corresponding controls in a 2 - year drinking water study.
Otoshi et al. 1993	Succinic acid, sodium succinate and disodium succinate were tested for their effects on cell proliferation and its subsequent influence on the development of bladder cancer in F344 rats. In experiment 1, male rats treated with the promoter N-butyl-N-(4-hydroxybutyl) nitrosamine for 4 weeks and ten received basal diets containing 5% of the acid or sodium salts for 32 weeks. In experiment 2 male rats received diets containing either 5% sodium succinate or 5% disodium succinate for 8 weeks. Tumor promotion was associated with sodium ion levels. The results indicate that succinic acid had no effect on promotion of carcinogenesis

8.6. GENOTOXICITY

Table 6. Results from genetic toxicity studies using succinic acid

Reference	Short description /Results
Ishidate et al. 1984.	Reverse mutation assays were carried out according to the pre-incubation method of Ames et al., 1975 with *Salmonella typhimurium* TA92, TA1535, TA100, TA1537, TA94, and TA98. Cells cultured overnight were pre-incubated with both the test substance and the S-9 mix for 20 minutes at 37°C before plating. Duplicate plates were used for each of 6 different concentrations of the sample. The number of revertant (his+) colonies was scored after incubation at 37°C for 2 days. The result was considered positive if the number of colonies found was twice the number in the control (phosphate buffer). Succinic acid was not mutagenic to *Salmonella typhimurium* TA92, TA1535, TA100, TA1537, TA94, and TA98, with and without polychlorinated biphenyl KC-400- treated rat liver S-9 at a maximum dose of 5.0 mg/plate (no other doses were specified). No significant increases in the number of revertant colonies were detected in any *S. typhimurium* strains at the maximum dose. Succinic acid was not mutagenic in these assays.
Ishidate et al. 1984.	Type: Chromosomal Aberration Test Cell Type: Chinese hamster fibroblasts The cells were exposed to the test substance at 3 different doses of succinic acid for 24 and 48 hours. The maximum dose was selected based on a preliminary test, in which the dose needed for 50% cell-growth inhibition was estimated using a cell densitometer. Untreated cells and solvent-treated (physiological saline) cells served as negative controls. The results were considered to be negative if the incidence was less than 4.9%, equivocal if it was between 5.0 and 9.9%, and positive if it was more than 10.0%. (Note: Metabolic activation was not employed.) There was 0% polyploid and 1.0% structural aberrations at 48 hours at the maximum dose tested. Succinic acid did not induce chromosomal aberrations in this assay.

9. Basis for Concluding that the Notified Use of Succinic Acid is GRAS

General recognition of safety based on scientific procedures requires that the substance as a whole be recognized as safe on the basis of a scientific evaluation of toxicity and level of use and that the scientific information for the assessment on which the finding is based be generally available (21 CFR 170.30). These two findings have already been established for succinic acid as demonstrated by it's GRAS status in 21 CFR 184.1091. In this notification we are only notifying a new method of production for the substance. The salient issue is whether that notified process is substantially equivalent to that made by the conventional process.

Analytical data described in this notification show that the impurities present in the BioAmber succinic acid are present at a very low level and primarily consist of components that also GRAS. Based on the totality of the evidence we conclude that succinic acid resulting from the BioAmber fermentation process is substantially equivalent to that made with the conventional process.

The information described above and the attached information considered, it is respectfully submitted that under the conditions of intended use, BioAmber's succinic acid is exempt from the premarket approval requirements of the Federal Food, Drug and Cosmetic Act because it is generally recognized as safe.

10. REFERENCES

PATENT APPLICATIONS

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APPENDIX 1

SPECIFICATIONS FOR BIO-BASED SUCCINIC ACID

BioAmber
CHEMISTRY INSPIRED BY NATURE

TECHNICAL DATA SHEET
BIO-BASED SUCCINIC ACID
NATURAL FLAVOR GRADE 99,5%

PRODUCER

BIOAMBER S.A.S
Route de Pomacle
51110 BAZANCOURT - France
Tel: +33 3 26 89 48 90
Web site: www.bio-amber.com

PACKAGING, STORAGE AND TRANSPORT

Packaging: 500-Kg big-bags, 25-kg bags
Storage: Two years in unopened original packaging in a dry place before re-certification
Transport: Not dangerous good as per US Gov. CFR 172.101

SPECIFICATIONS

CAS number:	110-15-6	Particle size:	98% <500µm
EINECS number:	203-740-4	Bio-based carbon:	> 97%
Molecular weight:	118.09 g/mol	Assay:	> 99,5% (Titration NaOH)
Melting point :	186°C – 190°C	Residue on Ignition:	< 0,025%
Boiling point:	235°C	Water content:	< 0,5%
Appearance:	white crystalline powder	Other organic acids:	< 0,2%
Lead:	< 1 mg/kg	Arsenic:	< 1 mg/kg
Mercury:	< 1 mg/kg		

Succinic acid is registered under REACH (01-2119896114-34-0001). Succinic acid (Flavis N° 08.024) meets Regulation EC N°1334/2008 on Natural Food Flavoring, Regulation EC N°1333/2008 and E363 of EU231/2012 on Food Additives and Regulation EC N°1831/2003 on Feed Additives. Succinic acid also meets the USP FCC monograph standard for purity. It is on the US Everything Added to Food in the United States list (EAFUS) and is accepted as a food additive (21 CFR 184.109) and a food flavor in the US. Succinic acid is a USDA certified bio-preferred product; for more information go to www.biopreferred.gov . It is certified Kosher by the Federation of Synagogues, UK and is produced using non-genetically modified feedstocks.

APPLICATIONS

Natural succinic acid can be used in a number of applications such as food, flavor, fine chemicals, etc. For more information, please contact BioAmber's representative or visit our web site at www.bio-amber.com.

Safety Data

Product SDS/eSDS are available on our web site at www.bio-amber.com and/or upon request at product info@bio-amber.com .

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APPENDIX 2

SDS FOR BIO-BASED SUCCINIC ACID

APPENDIX 3

NMR REPORT DETERMINING EQUIVALENCY BETWEEN PETRO-BASED AND BIO-BASED SUCCINIC ACID

APPENDIX 1

SPECIFICATIONS FOR BIO-BASED SUCCINIC ACID

BioAmber
CHEMISTRY INSPIRED BY NATURE

TECHNICAL DATA SHEET
BIO-BASED SUCCINIC ACID
NATURAL FLAVOR GRADE 99,5%

PRODUCER

BIOAMBER S.A.S
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PACKAGING, STORAGE AND TRANSPORT

Packaging: 500-Kg big-bags, 25-kg bags
Storage: Two years in unopened original packaging in a dry place before re-certification
Transport: Not dangerous good as per US Gov. CFR 172.101

SPECIFICATIONS

CAS number:	110-15-6	Particle size:	98% <500µm
EINECS number:	203-740-4	Bio-based carbon:	> 97%
Molecular weight:	118.09 g/mol	Assay:	> 99,5% (Titration NaOH)
Melting point :	186°C – 190°C	Residue on Ignition:	< 0,025%
Boiling point:	235°C	Water content:	< 0,5%
Appearance:	white crystalline powder	Other organic acids:	< 0,2%
Lead:	< 1 mg/kg	Arsenic:	< 1 mg/kg
Mercury:	< 1 mg/kg		

Succinic acid is registered under REACH (01-2119896114-34-0001). Succinic acid (Flavis N° 08.024) meets Regulation EC N°1334/2008 on Natural Food Flavoring, Regulation EC N°1333/2008 and E363 of EU231/2012 on Food Additives and Regulation EC N°1831/2003 on Feed Additives. Succinic acid also meets the USP FCC monograph standard for purity. It is on the US Everything Added to Food in the United States list (EAFUS) and is accepted as a food additive (21 CFR 184.109) and a food flavor in the US. Succinic acid is a USDA certified bio-preferred product; for more information go to www.biopreferred.gov . It is certified Kosher by the Federation of Synagogues, UK and is produced using non-genetically modified feedstocks.

APPLICATIONS

Natural succinic acid can be used in a number of applications such as food, flavour, fine chemicals, etc. For more information, please contact BioAmber's representative or visit our web site at www.bio-amber.com.

Safety Data

Product SDS/eSDS are available on our web site at www.bio-amber.com and/or upon request at product info@bio-amber.com .

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APPENDIX 2

SDS FOR BIO-BASED SUCCINIC ACID

1. IDENTIFICATION

1.1. Product identification

Product Name	Bio-based succinic acid
Chemical name	succinic acid butanedioic acid
CAS number	110-15-6
EC number	203-740-4

1.2. Relevant identified uses of the substance or mixture and uses advised against

Applications	Intermediate
Identified uses	Manufacture via a fermentation procedure Industrial distribution Formulation (chemical products for water treatment) Formulation (welding products) Final industrial use (pH regulator, flocculating agent, precipitant, neutralisation agent, other non-specified) Final industrial use (water treatment) Final industrial use (welding products) Final industrial use (monomeric) Final industrial use (intermediate in a formulation) Final industrial use (esterification and other synthesis processes) Final industrial use (hydrogenation) Final industrial use (food additives)

1.3. Details of the supplier of the safety data sheet

Name	BIOAMBER S.A.S
Address	Route de Pomacle 51110 BAZANCOURT - FRANCE
Phone	+33 (0)3 26 89 48 90
Contact email	info@bio-amber.com

1.4. Emergency phone number

For Hazardous Materials Incidents Spill, Leak, Fire, Exposure, or Accident	Call CHEMTREC Day or Night Within USA and Canada: 1-800-424-9300 Outside USA and Canada: +1 703-527-3887 (collect calls accepted)

2. HAZARD IDENTIFICATION

2.1. Classification of the substance

2.1.1. Classification of the substance according to OSHA HCS 2012

Eye Damage Category 1 Causes serious eye damage

2.1.2. Classification of the substance according to HMIS Classification

Health hazard:	2
Flammability:	0
Physical hazards:	0

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2.1.3. Classification of the substance according to NFPA Rating

Health:	2
Flammability:	0
Instability:	0

2.1.4. Classification of the substance according to WHMIS

Class D2B (eye irritation)

2.2. Labelling elements according to OSHA HCS 2012

Symbol

Signal word	Danger
Hazard statement	Causes serious eye damage
Precaution statements	Wear eye protection/face protection. If in eyes: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a physician.

2.3. Other dangers

Potential effects on health (not fulfilling the criteria for classification):

Inhalation: May be harmful if inhaled. Causes respiratory tract irritation.

Cutaneous: May cause skin irritation.

Ingestion: May be harmful if swallowed.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	Common name/Synonyms	CAS number	EC number	[%]
Succinic acid	Butanedioic acid Bio-based succinic acid	110-15-6	203-740-4	98-100

4. FIRST AID MEASURES

4.1. First aid description

General instructions	Consult a doctor. Show this safety data sheet to the doctor to help him/her provide the right assistance. Move away from the danger zone.
If inhaled	If inhaled, get the person in question into fresh air. If they are no longer breathing, perform artificial respiration. Consult a doctor.
In the event of skin contact	Rinse with soap and plenty of water. Consult a doctor.

In the event of contact with the eyes	Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a physician.
If ingested	Never administer anything by mouth to an unconscious person. Rinse the mouth with water. Consult a doctor.

4.2. Principal symptoms and effects, both acute and delayed

Eye contact will result in strong irritation. No known delayed effects.

4.3. Indication of any immediate medical attention and special treatment needed

Treat symptomatically.

5. FIREFIGHTING MEASURES

5.1. Extinguishing methods	Appropriate: water jet, alcohol-resistant foam, dry chemical products or carbon dioxide.
5.2. Specific hazards from the substance or mixtures	Hazardous decomposition products formed under fire conditions - Carbon oxides
5.3. Special protective equipment and precautions for fire-fighters	Wear self-contained breathing apparatus if necessary.

6. ACCIDENTAL RELEASE MEASURES

6.1. Personal precautions, protective equipment and emergency procedures	Use personal protection equipment. Avoid producing dust. Avoid breathing in dust. Ensure that ventilation is adequate.
6.2. Environmental protection precautions	Do not let the product get into the drains.
6.3. Methods and materials for containment and cleaning	Gather and dispose of without creating dust. Store in closed containers that are appropriate for disposal.

7. HANDLING AND STORAGE

7.1. Precautions to be taken for safe handling	Avoid contact with skin and eyes. Avoid producing dust or aerosols. Provide appropriate ventilation in locations where dust is generated. The usual preventive measures for protecting against fire.
7.2. Safe storage conditions, including any incompatibilities	Use tightly sealed containers and store them in a dry and well-ventilated space.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

Exposure limits	OSHA: Not established ACGIH: Not established

8.2. Personal protection

Appropriate engineering measures	No special ventilation requirements. Good general ventilation should be sufficient to control worker exposure to airborne contaminants.
Personal protection equipment	Eye/face protection: Wear eye protection/face protection. Skin/hand protection: Wear gloves when handling. Select bodily protection measures depending on the quantity and concentration of the hazardous substance in the workplace. Respiratory protection: If the risk assessment shows that gas masks with air purifying filters are appropriate, use a type N95 mask (US) or a type P3 (EN 143) respirator. Use masks that have been tested and approved to the appropriate standards such as NIOSH (US) or CEN (EU). Hygiene measures: Handle in accordance with industrial good hygiene and safety practices. Wash hands before breaks and at the end of the day.

9. PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information about the essential physical and chemical properties

Physical state	Powder
Colour	White
Odour	Odourless
Olfactory threshold	Not determined
pH	2.4 to 2.8 (1% aqueous solution)
Melting point/freezing point	185 to 187°C
Boiling point	235°C
Flash point	Not applicable. The flash point is a property that is relevant for liquids and solids with low melting points. Succinic acid has a melting point above 185°C.
Evaporation rate	Not determined
Flammability (solid, gas)	Succinic acid is non-flammable. Practical experience with this substance has shown that succinic acid is not pyrophoric and does not emit flammable gases when it comes into contact with water.
Upper/lower flammability limits or explosive limits	Not determined
Vapour pressure	0.000025 Pa (25°C)
Vapour density	Not determined
Relative density	1.57 (at 20°C)
Solubility in water	83 g/L (at 25°C)

In other solvents	Not determined
Partition coefficient: *n*-octanol/water	Log K_{ow}: -0.59
Auto-ignition temperature	No auto-ignition temperature could be determined up to 220°C, a temperature that is already above the melting point.
Decomposition temperature	Not determined
Viscosity	Not applicable. Succinic acid is a solid.
Explosive properties	Not applicable. Succinic acid does not contain any chemical groups that are associated with explosiveness. Succinic acid is not expected to be sensitive to static discharge.
Oxidising properties	Not applicable. Succinic acid does not contain any chemical structures that would suggest oxidising properties.

9.2. Other information

Kst, Pmax: Kst = 51 bar.m/s - Pmax = 7.4 bar

Minimum energy for inflammability > 1000 mJ

Inflammability temperature (cloud) min. 620°C

10. STABILITY AND REACTIVITY

10.1. Reactivity	Succinic acid does not become liquid during transport. It is therefore exempt from corrosiveness tests with respect to metals.
10.2. Chemical stability	Stable under the recommended storage conditions.
10.3. Potential for dangerous reactions	Under normal conditions of storage and use, hazardous polymerization will not occur
10.4. Conditions to be avoided	Not available.
10.5. Incompatible materials	Bases, oxidising agents, reducing agents
10.6. Dangerous decomposition products	In the event of a fire: carbon dioxide and carbon monoxide

11. TOXICOLOGICAL INFORMATION

11.1. Information about toxicological effects

Routes of Entry	Inhalation, ingestion, and dermal and eye contact

Acute toxicity	The acute toxicity of succinic acid is low: - oral: Results of studies into rats by Fisher 344 (Guideline OECD 401) LD_{50} (rat, oral): 6740 mg/kg bw - cutaneous: Not determined - inhalation: Results of studies into rats by Sprague-Dawley (Guideline OECD 403) LC_{50} (rat, inhalation): 1284 mg/m³ air
Skin corrosion/skin irritation	Results of studies into rabbits (Guideline OECD 404, EU B.4): not irritant.
Severe eye injuries/eye irritation	Results of studies into rabbits (Guideline OECD 405, EU B.5): strong irritant.
Respiratory or cutaneous sensitisation	Respiratory: Comparative reading of the results for fumaric acid indicates that there will be no topical effects on the respiratory system. Cutaneous: *Local lymph node assay* (LLNA): non-sensitising *Guinea pig maximisation test* (GPMT): non-sensitising
Stem cell mutagenicity	Result of the Ames test: negative Result of the chromosomal aberration test: negative
Carcinogenicity	Results of studies into rats by Fisher 344 (Guideline OECD 451): comparative reading of the results for succinate indicates there will be neither toxicity nor carcinogenic activity. $NOAEL_{oral}$: 860 mg/kg bw/day NTP: Not listed IARC: Not listed OSHA: Not listed
Reproductive toxicity	There are no indications of any toxicity in terms of reproduction or development.
Teratogenicity/Embryotoxicity	There are no indications of any toxicity in terms of teratogenicity or embryotoxicity.
Specific toxicity for various target organs - single exposure	Not determined
Specific toxicity for various target organs - repeated exposure	Oral: Results of studies into rats (Guideline OECD 408): NOAEL: 860 mg/kg bw/day (chronic; rat)
Hazards due to aspiration	Not applicable. Succinic acid is a solid.
Toxicologically Synergistic Materials	Not available

11.2. Potential health effects

Inhalation	May be harmful if inhaled. Causes respiratory tract irritation.
Ingestion	May be harmful if swallowed.
Cutaneous	May cause skin irritation.

Eye	Strong irritant. Causes serious eye damage.

12. ECOLOGICAL INFORMATION

12.1. Toxicity

No dangers have been identified at biologically relevant concentrations.

Aquatic toxicity

Acute toxicity, fish (Guideline OECD 203):
LC_{50} fresh water (*Danio rerio*) 96h >100 mg/L.

Acute toxicity, invertebrates (Guideline OECD 202):
EC_{50} 48h fresh water (*Daphnia magna*) in a test with pH adjustment >100 mg/L.

Acute toxicity, algae (Guideline OECD 201):
EC_{50} 72h fresh water (*Pseudokirchnerella subcapitata*) >100 mg/L.
NOEC 100 mg/L.

Toxicity to micro-organisms (Guideline OECD 209):
EC_{50} 3h fresh water (activated sludge) >300 mg/L.

12.2. Persistence and degradability

Results of a study into biodegradability in water (Guideline OECD 301 E): easily biodegradable

12.3. Bioaccumulation potential

Log Kow < 4.5: non-bioaccumulating

12.4. Mobility in the soil

The substance only has a weak adsorption potential

12.5. Results of PBT and vPvB evaluations

The substance is neither persistent, nor bioaccumulating, nor toxic

12.6. Other undesirable effects

None known.

13. DISPOSAL CONSIDERATIONS

13.1. Waste handling methods

Respect the regulations in force. Contact an accredited service professional for disposal of this product.
Contaminated packaging: dispose of with unused product

14. INFORMATION FOR TRANSPORT

	Transport by land (ADR/RID)	Transport by river (ADN)	Transport by sea (IMDG)	Transport by air (ICAO-TI / IATA-DGR)
14.1. UN number	Not regulated for transport			
14.2. UN shipping name	Not regulated for transport			
14.3. Hazard class or classes	Not regulated for transport			
14.4. Packaging group	Not regulated for transport			

14.5. Environmental hazards:	Not regulated for transport
14.6. Classification	Non-hazardous goods
14.7. Additional information	Not regulated for transport

14.8. Specific precautions to be taken by the user
Not Available

14.9. Bulk transport in accordance with Appendix II of MARPOL 73/78 and the IBC Code
Not Applicable

15. REGULATORY INFORMATION

Regulations/legislation specific to the substance or mixture regarding safety, health and the environment

Canada:
WHMIS: Class D2B (Eye irritation)

- DSL Status: All the components of this product can be found on the Canadian DSL list
This product has been classified in accordance with the hazard criteria of the *Controlled Products Regulations* and the MSDS contains all the information required by the *Controlled Products Regulations*.

USA:

This product has been classified in accordance with the 2012 hazard criteria of the *Occupational Safety and Health Administration's (OSHA) Hazard Communication Standard (HCS)* and the SDS contains all the information required by the 29 CFR § 1910.1200 .
- SARA 302: None of the chemical components of this material are subject to the reporting requirements of SARA Title III, Section 302.

- SARA 313: This material does not contain any CAS chemical constituents that are known to exceed the threshold established by SARA Title III, Section 313.

- SARA 311/312 Hazards: Acute Health Hazard

- Massachusetts Right To Know Components: None of the chemical components of this material are subject to the requirements of the Massachusetts Right to Know Act.

- Pennsylvania Right To Know Components
Succinic acid:
CAS number
110-15-6
Revision Date

- New Jersey Right To Know Components:
Succinic acid
CAS number
110-15-6
Revision Date

- California Prop. 65 Components:
This product does not contain any chemical substances known in the

state of California to cause cancer, congenital malformations or any other reproductive damage.

16. OTHER INFORMATION

16.1. Information about the revision

SDS created on 22/06/2012.

16.2. Meanings of the abbreviations and acronyms used

ACGIH: American conference of Governmental Industrial Hygienists
ADN/ADNR: regulations relating to the transportation of hazardous substances in barges on navigable waterways
ADR/RID: European agreement relating to international transport of hazardous goods by road/regulations relating to the international transport of hazardous goods by rail
CAS number: Chemical Abstract Service number
CEN: European Committee for Standardisation
CLP: classification, labelling and packaging
DSL: Domestic Substances List
EC number: European Commission number
EC_{50}: Effective Concentration – 50%
EU: European Union
HCS: Hazard Communication Standard
HMIS: Hazardous Material Information System
IARC: International Agency for Research on Cancer
IATA-DGR: International Air Transport Association – Dangerous Goods Regulations
IBC: International Bulk Chemical
ICAO-TI: International Civil Aviation Organization - Technical Instructions
IMDG: International Maritime Dangerous Goods Code
LC_{50}: Lethal Concentration – 50%
LD_{50}: Lethal Dose – 50%
MARPOL: International Convention for the Prevention of Pollution From Ships
MSDS: Material Safety Data Sheet
NFPA: National Fire Protection Association
NIOSH: National Institute for Occupational Safety and Health
NOAEL: No Observed Adverse Effect Level
NOEC: No Observed Effect Concentration
NTP: National Toxicology Program
OECD: Organisation for Economic Co-operation and Development
OSHA: Occupational Safety and Health Administration
PBT: Persistent Bioaccumulative Toxic Substances
Prop.: Proposition
SARA: Superfund Amendments and Reauthorization Act
SDS: Safety Data Sheet
UN number: United Nations number
vPvB: very Persistent and very Bioaccumulative
WHMIS: Workplace Hazardous Material Information System

The information contained in this file is based on our current state of knowledge and has been provided in accordance with the applicable European directives. This information is provided in order to give the characteristics of the product and to assist in applying safety instructions. However, this document does not constitute any warranty, express or implicit, regarding the properties of the product.

APPENDIX 3

NMR REPORT DETERMINING EQUIVALENCY BETWEEN PETRO-BASED AND BIO-BASED SUCCINIC ACID

FILAB

Société ECO MUNDO
A l'attention de Mme LEVAS Leslie
215, rue Jean-Jacques Rousseau
92136 ISSY LES MOULINEAUX

Dijon, January 23rd, 2012

Report n°17843
Quote : T12010101 dated January 11th, 2012

RE : MNR 1H and 13C{1H}* Analyses

* Analysis performed by an affiliate laboratory.

1) Purpose

Characterization of a sample of succinic acid by 1H et 13C{1H} Nuclear Magnetic Resonance.

2) Samples

Internal reference : 11wpcm_03579_RMN référence FILAB : 17843-42779

3) Analysis

a/ Equipment

Analyses were performed on a RMN RMN 300 MHz Bruker spectrophotomerer equipped with a BBOF sensor at room temperature (300°K).

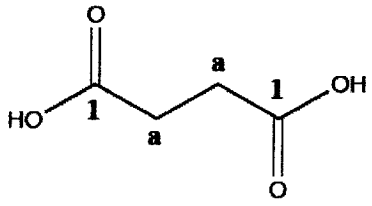
b/ Sample preparation

Samples containing about 10 mg of product was diluted in DMSO-d6 and introduced in a NMR 5 mm tube.

c/ Results

Les spectres RMN obtenus sont présentés en annexe.MNR spectra obtained are presented in Appendix (Annexes).

Table 1 : Table showing different MNR 1H and 13C signals.



FILAB SAS
Parc Mazen Sully - 13, Rue Pauline Kergomard - BP 37460 - 21074 DIJON – Tél.: 03 80 52 32 05 - Télécopie : 03 80 52 01 11-
e-mail : contact@filab.fr- RCS DIJON 491 631 891 - S.A.S. au capital de 135 000 Euros.

FILAB

	Spectre 1D ^{1}H				Spectre 1D ^{13}C	
	δ (ppm)	nb de 1H	multiplicité		δ (ppm)	
a	2,408	4	(s)	**A**	28,7	2 CH2
OH	12,07	2	(s) large	**1**	173,6	2 CO

Spectra are comparable to those found in the SDBS spectra bank (ref 2001) corresponding with succinic acid.

4) Conclusion

Spectra obtained were identical to the structure of succinic acid.

Visa
Coordinatrice Technique

Valérie LASSEIGNE

(b) (6)

Visa
Chargé de Mission
Développeur Analytique

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(b) (6)

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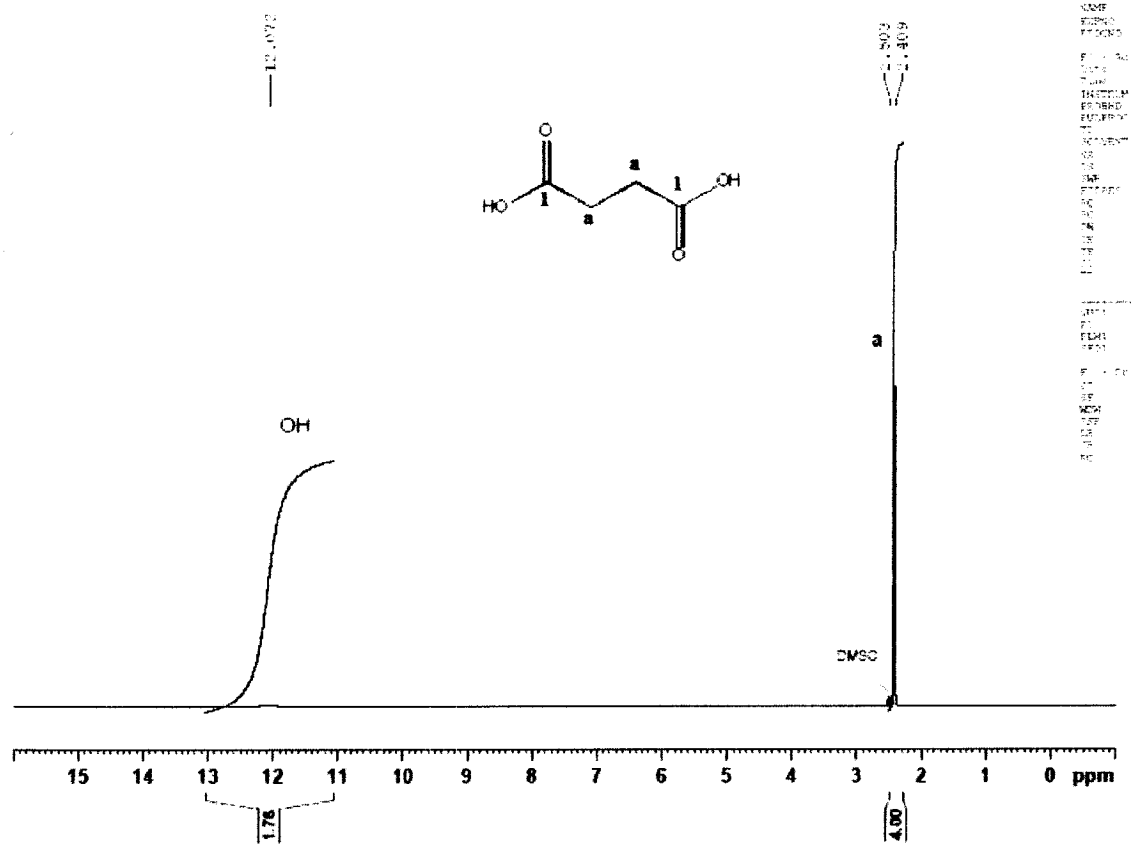
Annexes

17343-42779



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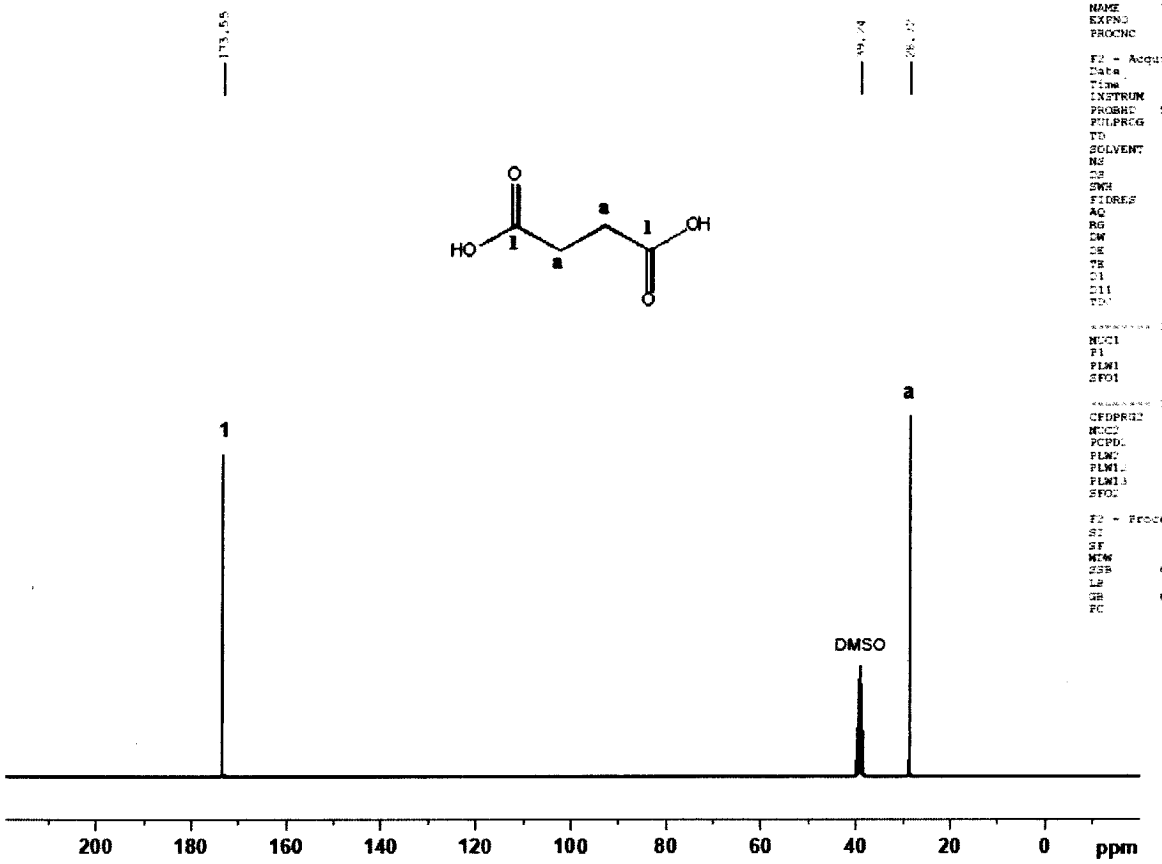
Laboratoires d'analyses industrielles

17843-42779




```
Current Data Parameters
NAME        12mfp wpcm18579
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_              20120118
Time                 21.13
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
SWH              18028.846 Hz
FIDRES           0.275098 Hz
AQ               1.8175898 sec
RG                    12.1
DW                  27.733 usec
DE                   6.50 usec
TE                  299.9 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                    9.00 usec
PLW1           35.00000000 W
SFO1           75.4752949 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2                 90.00 usec
PLW2           0.22000000 W
PLW12          0.19494999 W
PLW13          0.14981000 W
SFO2           300.1312005 MHz

F2 - Processing parameters
SI                    32768
SF             75.4672986 MHz
WDW                     EM
SSB                     0
LB                    1.00 Hz
GB                      0
PC                    1.40
```

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SUBMISSION END